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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/812,502	03/20/2001	Marilyn Anne Anderson	9748BZ	7221

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EXAMINER
SAIDHA, TEKCHAND

ART UNIT	PAPER NUMBER
1652	14

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)	
09/812,502	Anderson et al.	
Examiner	Group Art Unit	
T. Saidha	1652	14

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 3/28/03 (TD).

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 33-38 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) 36 is/are allowed.

☒ Claim(s) 33-35 & 37-38 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Action Summary

1. The terminal disclaimer filed on 3.28.03 (Paper No. 13) disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S.P. 6,261,821 has been reviewed and is accepted. The terminal disclaimer has been recorded.

2. Applicants' Amendment filed 11.26.02 (Paper No. 9) and Supplemental Amendment dated 3.28.03 (Paper No. 12) have been entered. Claims 33-38 are pending and under consideration in this examination.

3. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed as per the amendment cited as per Paper No. 9 and in view of new claims 33-38 currently pending have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).

5. ***Sequence Rules***

The instant specification on pages 9 (line 33), page 10 (lines 7, 11 & 27) & page 11 (line 10), present amino acid sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), but fails to comply with the requirements. According to 37 CFR 1.821-825, every disclosed amino acid sequence of **four or more residues** or 10 or more nucleotides must be identified by a SEQ ID NO. The amino acid sequences presented do not have SEQ ID Nos. In order to comply with the sequence rules Applicants must identify these sequences by providing SEQ ID NO :, and where required provide a new version of the sequence listing and disk.

The sequences present in claims 33 & 34 lack description by the appropriate sequence identifier as required by 37 CFR § 1.821(d). **Figures 9b and 10** also present sequences that are encompassed by the definition of amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), but fails to comply with the requirements. According to 37 CFR 1.821-825

Applicants argue that the claimed sequences are characterized as a structure instead of an amino acid sequence. However, this pending claims 33-34 continue to recite 'consisting of amino acid sequence' as well as the figures present sequences without sequence identifiers or SEQ ID Nos. Hence compliance with the sequence rules is required.

6. ***Written Description***

Claims 33-35 & 37-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 33-35 & 37-38 are directed to any protease sensitive peptide or a nucleic acid encoding such a peptide 'the claimed genus', wherein X_1 & X_2 may be the same or different amino acid residues but preferably 'Lys' residues; and wherein R_1 & R_2 may be any of the amino acid residue or a peptide. The specification on page 10, lines 1-3 assumes that such a discovery of a protease sensitive peptide will enable the engineering of peptides and polypeptides capable of being processed in a plant by cleavage. No specific examples are presented, however. The prior art is silent about such or similar constructs that a skilled artisan could use in order to practice

such an invention. The specification does not describe in clear terms even a single or representative number of species to the genus. A 'representative number of species' requires that the species which are expressly described be representative of the entire genus. Therefore, without a clear description of even a single functional protease sensitive peptide construct or the nucleic acid encoding the same, further modification that are expected to be made in substituting the R_1 & R_2 or X_1 & X_2 for other compounds would require adequate written description of the genus, which cannot be achieved by disclosing a generalized genus. In an unpredictable art, such as the instant one, wherein a peptide construct and the nucleic acid encoding such a construct - be made by amino acid or peptide group substitution, adequate written description requirement of a genus cannot be achieved by disclosing a generic formula without clear-cut identifying characteristics, such as structure or functional activity of the peptide construct or nucleic acid encoding the same, written description for each member within the genus will be necessary and such is not described. Therefore, the written description requirement is not satisfied.

Applicants arguments :

Applicants argue that the specification describes the general structure : R1-X1-X2-Asn-Asp-R2. The specification further provides an example of such a protease sensitive peptide of SEQ ID NO : 3 (protease inhibitor (PI) precursor) which is cleaved at six sites to produce seven peptides.

In response Applicants' SEQ ID NO : 3 is a 368 amino acid sequence which having cleavable sites is cleaved at six sites to produce seven peptides. Therefore, SEQ ID NO : 3 is the

protease sensitive peptide and not the seven peptides. The seven peptides being the product of the cleavage.

7. ***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 33-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Williams [U.S.P. 5,032,396, July 16, 1991]. Williams teaches a peptide sequence (see Table 2) comprising the amino acid sequence : .....GLN-**LYS-LYS-ASN-ASP**-ALA..... [where X_1 & X_2 are Lys residues and R_1 are amino acid(s) GLN or residues 1-102 ; & R_2 are amino acid(s) ALA or residues 107-129] which by virtue of the structure is functionally a protease sensitive peptide, because protease acts between residues Asn-Asp. The claims are written so broadly as to be anticipated by the reference.

8. ***New Rejection***

Claims 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Sigma Peptides : Product Nos : T-5028 or T-5153 [Nature 321, 441 (1986)] or A-7907 [PNAS, USA., 79, 1443 (1982)].

T 5028 - TYR- ALA-GLY-ALA-VAL- **ASN- ASP** -LEU

T-5153 - TYR- GLY-ALA-VAL-VAL- **ASN- ASP** -LEU

A-7907 - ARG-ARG-LEU-ILE-GLU- **ASP-ASN** -GLU-TYR-THR-ALA-ARG-GLY

These peptides when read in the light of the claim limitations read upon the claims. As recites in claims 33-34, X1 and X2 can be the same or different amino acid residues - which may be more than one amino acid at each of the positions, which is clearly the same at the Sigma peptides, and being the same inherently qualify to be a protease-sensitive peptide. The other limitations of claims 33-34 are R2 which may be an amino acid or a peptide which is represented by the underlined amino acid LEU in Product Nos. T 5028 or T-5153; or the peptide -GLU-TYR-THR-ALA-ARG-GLY in Product Nos. A-7907, and is therefor anticipated.

9. ***Claim Rejections - 35 U.S.C. § 103***

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suggs et al. [Suggs et al.[PNAS, USA.,78(11) : 6613-6617] in view of Williams [U.S.P. 5,032,396, July 16, 1991].

Suggs et al. teach the use of mixtures of chemically synthesized oligodeoxyribonucleotides as hybridization probes for the isolation of specific cloned DNA sequences. The approach is to "chemically synthesize a mixture of oligonucleotides that represent all possible codon

combinations for a small portion of the amino acid sequence of a given protein." Once a protein, in this case the protease of the generalized structure (R1-**X1- X2 -ASN-ASP**- R2) or the specific sequence [GLN-**LYS-LYS-ASN-ASP**-ALA] of Williams, is purified and known. Under the principle that one sequence must be complementary to the DNA for that protein, "the complementary oligonucleotide will form a perfectly base paired duplex with the DNA from the coding region...". Thus, mixed oligonucleotide probes allow the isolation of DNA sequences for any protein with a known or obtainable portion of the amino acid sequence.

In light of the method of Suggs et al. for isolating the appropriate DNA sequence coding for a particular protein, it would have been obvious to one of ordinary skill in the art to use these methods to determine the coding nucleotide sequence of protease in murine (IL-7) disclose the fact that murine produces the protease and therefore possesses that gene. The state of the art at the time the invention was made dictates that, since the culturing and recovery of the naturally-occurring enzyme from its natural source yields small, and at times unstable, amounts, production of such proteins by recombinant means is the single best technique to dramatically increase yield and insure stable production of the protein. One would not have to probe a library of possible sources to find a similar gene, as Williams provides sufficient motivation to merely determine the sequence from the known source. Thus, the nucleic acid molecule of the claim 23 is not considered patentable.

From this, one utilizing the ordinary level of skill in the art could easily assemble various expression vectors containing either a recovered full length clone, or the appropriate fragments

ligated at the corresponding restriction sites. The transformation of host cells with this vector is also within the ordinary skill in the art, as a variety of cell lines, both prokaryotic and eukaryotic, human (mammalian) included, are well documented and commonly used. The selection of the appropriate plasmids, promoters, and cell lines for proper expression of the inserted gene is merely a matter of judicious selection, within the scope of ability of one ordinarily skilled in the art.

10. ***Double Patenting***

In view of Applicants filing of Terminal Disclaimer, the Double Patenting rejection previously made based upon U.S.P. 6,261,821, is withdrawn.

11. Applicants' further arguments do not relate to the claims as amended and filed as per the 'supplemental amendment', dated 3.28.03 (Paper No. 12) and is therefore not responded to.

12. Claim 36 is allowed

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (703) 305-6595. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group in the Technology Center is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

T. Saidha

Tekchand Saidha
Primary Examiner, Art Unit 1652
April 23, 2003